AMENDMENT OF SOLICITATION/MODIFICATION OF CONTRACT

1. CONTRACT ID CODE	PAGE OF PAGES
	1 | 8

2. AMENDMENT/MODIFICATION NO.	3. EFFECTIVE DATE	4. REQUISITION/PURCHASE REQ. NO.	5. PROJECT NO. *(If applicable)*
0001	See Block 16C		

6. ISSUED BY CODE ASPR-BARDA

ASPR-BARDA
200 Independence Ave., S.W.
Room 640-G
Washington DC 20201

7. ADMINISTERED BY *(If other than Item 6)* CODE ASPR-BARDA02

US DEPT OF HEALTH & HUMAN SERVICES
ASST SEC OF PREPAREDNESS & RESPONSE
ACQ MANAGEMENT, CONTRACTS, & GRANTS
O'NEILL HOUSE OFFICE BUILDING
Washington DC 20515

8. NAME AND ADDRESS OF CONTRACTOR *(No., street, county, State and ZIP Code)*

REGENERON PHARMACEUTICALS, INC. 1466256
777 OLD SAW MILL RIVER RD
TARRYTOWN NY 105916717

CODE 1466256 FACILITY CODE

(x) **9A. AMENDMENT OF SOLICITATION NO.**

9B. DATED *(SEE ITEM 11)*

x **10A. MODIFICATION OF CONTRACT/ORDER NO.** HHSO100201700020C

10B. DATED *(SEE ITEM 13)* 09/21/2017

11. THIS ITEM ONLY APPLIES TO AMENDMENTS OF SOLICITATIONS

☐ The above numbered solicitation is amended as set forth in Item 14. The hour and date specified for receipt of Offers ☐ is extended. ☐ is not extended.
Offers must acknowledge receipt of this amendment prior to the hour and date specified in the solicitation or as amended, by one of the following methods: (a) By completing Items 8 and 15, and returning _____ copies of the amendment; (b) By acknowledging receipt of this amendment on each copy of the offer submitted; or (c) By separate letter or telegram which includes a reference to the solicitation and amendment numbers. FAILURE OF YOUR ACKNOWLEDGEMENT TO BE RECEIVED AT THE PLACE DESIGNATED FOR THE RECEIPT OF OFFERS PRIOR TO THE HOUR AND DATE SPECIFIED MAY RESULT IN REJECTION OF YOUR OFFER. If by virtue of this amendment you desire to change an offer already submitted, such change may be made by telegram or letter, provided each telegram or letter makes reference to the solicitation and this amendment, and is received prior to the opening hour and date specified.

12. ACCOUNTING AND APPROPRIATION DATA *(If required)*
See Schedule

13. THIS ITEM ONLY APPLIES TO MODIFICATION OF CONTRACTS/ORDERS. IT MODIFIES THE CONTRACT/ORDER NO. AS DESCRIBED IN ITEM 14.

CHECK ONE	
	A. THIS CHANGE ORDER IS ISSUED PURSUANT TO: *(Specify authority)* THE CHANGES SET FORTH IN ITEM 14 ARE MADE IN THE CONTRACT ORDER NO. IN ITEM 10A.
	B. THE ABOVE NUMBERED CONTRACT/ORDER IS MODIFIED TO REFLECT THE ADMINISTRATIVE CHANGES *(such as changes in paying office, appropriation date, etc.)* SET FORTH IN ITEM 14, PURSUANT TO THE AUTHORITY OF FAR 43.103(b).
	C. THIS SUPPLEMENTAL AGREEMENT IS ENTERED INTO PURSUANT TO AUTHORITY OF:
X	Other Transaction Authority
	D. OTHER *(Specify type of modification and authority)*

E. IMPORTANT: Contractor ☐ is not. ☒ is required to sign this document and return 1 copies to the issuing office.

14. DESCRIPTION OF AMENDMENT/MODIFICATION *(Organized by UCF section headings, including solicitation/contract subject matter where feasible.)*

Tax ID Number: 13-3444607
DUNS Number: 194873139
IGF::OT::IGF - Regeneron Other Transaction Authority (OTA) Award
Period of Performance: 09/25/2017 to 05/31/2021

See "DESCRIPTION OF CHANGES"

Except as provided herein, all terms and conditions of the document referenced in Item 9 A or 10A, as heretofore changed, remains unchanged and in full force and effect.

15A. NAME AND TITLE OF SIGNER *(Type or print)*	16A. NAME AND TITLE OF CONTRACTING OFFICER *(Type or print)*
Joseph J. LaRosa, SVP + General Counsel	SALIM K. ROBERTS
15B. CONTRACTOR/OFFEROR (b) (6) *(Signature of person authorized to sign)*	15C. DATE SIGNED 9/28/18
16B. UNITED STATES OF AMERICA (b) (6) *(Signature of Contracting Officer)*	16C. DATE SIGNED 9-28-2018

As referenced in SECTION SF 30 BLOCK 14

DESCRIPTION OF CHANGES:

1. ATTACHMENT1: STATEMENT OF WORK, is hereby deleted and replaced as follows:

ATTACHMENT 1:
STATEMENT OF WORK (18 September 2018)

1. EXECUTIVE SUMMARY

Regeneron Pharmaceuticals, Inc. is submitting this Statement of Work (SOW) to develop novel antibodies against Pre-Emerging Pathogens (PEP), which can be re-directed in the face of an established public health threat to address an Emerging Pathogen (EP) or a Re-Emerging Pathogen (REP). The first program has the objective to advance the development of antibodies for treatment of influenza disease that have superior properties to products currently in development. The remaining pathogens will be prioritized by BARDA and Regeneron. The objectives of this proposal are founded upon Regeneron's proprietary VelociSuite® and other proprietary platform technologies, which enable rapid generation, screening, and production of fully human therapeutic candidates.

2. STATEMENT OF WORK

2.1. Preamble

Over the last decade, newly emerging (and re-emerging) infectious diseases have threatened the populations of the US and the rest of the world. Timely production of medical countermeasures to prevent and/or treat these threats has created a significant challenge for both the public and private sectors. For most classes of drugs, rapid development of therapeutics to treat emerging infections is impeded by the timelines needed to identify compounds with desired efficacy, safety and pharmacokinetic (PK) profiles in the clinic. Fully human monoclonal antibodies (mAbs) are molecules with high potency, predictable PK, and limited off-target toxicity and thus provide attractive types of therapeutics for emerging diseases. Importantly, we have repeatedly demonstrated that candidate mAb-based drugs to prevent and/or treat emerging infections can be rapidly obtained from Regeneron's proprietary VelocImmune® mice. Further, our ability to concurrently generate isogenic cell lines that are optimized for rapid antibody scale up and manufacturing [using our proprietary CMC platform technologies] have facilitated both testing of our mAbs in preclinical models and subsequent development of these mAbs into drugs suitable for human testing. In the process of completing many of these activities we have collaborated with other entities (including BARDA, Research Institutes, Government

Laboratories and Universities).

This document lays out our plans to ensure the success of future emergency response activities guided by a Joint Oversight Committee comprised of Regeneron and BARDA, and performed through a Consortium comprised of entities who have participated in our previous efforts, as well as selected entities that can provide key contributions to future efforts in the important task of providing medical countermeasures to treat emerging threats. Consortium membership will be key to the success of this program. In addition to the activities that will include Consortium members, research and development activities may employ Contract Research Organizations such as (b) (4) and Clinical Research Organizations like (b) (4) with which Regeneron has Master Services Agreements (MSA) already. Consortium members will be key to the success of this program and formal inclusion of these and other members in the Consortium will happen during the finalization of the framework contemplated by this Agreement. We envision a flexible process in which Consortium members are initially selected by Regeneron and added with the approval of BARDA and the formation of agreements with Regeneron. The Consortium will be led by Regeneron.

Consortium activities will be overseen by an Oversight Committee, which will be responsible for interrogating risks and progress of assets covered under this Agreement, endorse potential new assets, and propose modifications to the allocation of funding across activities covered under this Agreement. The Oversight Committee will be co-chaired by BARDA and Regeneron. Membership will include Regeneron and BARDA.

The activities described in this Statement of Work include an initial program plan focused on drugs to treat diseases caused by emerging and re-emerging pathogens, such as influenza virus and other emerging pathogens as determined by the Oversight Committee with agreement of Regeneron. Specifically, the Oversight Committee will establish programs to systematically identify key threats, defined as Pre-Emergent Pathogens (PEP), and the Consortium will commit resources to early development work on these target diseases to build a portfolio of drug candidates that can be rapidly advanced when needed upon agreement of the Oversight Committee, Regeneron and BARDA. Importantly, the Consortium will be structured in such a manner that resources allocated to work on PEPs can be redirected to rapidly address an emerging pathogen (EP) or reemerging pathogen (REP).

2.2. Overall Objectives and Scope

This initial program plan has an objective to advance the development of antibodies for treatment of influenza disease and to establish a program to develop novel antibodies against PEP, which can be re-directed in the face of an established public health threat to address an EP or a REP. Ongoing work on PEP, which will advance drug candidates that are likely to be needed during the course of the contract, will help to ensure the availability of resources in the face of a public health threat produced by an EP or REP.

All development programs are defined by discrete work Periods/Stages, including generating, validating, and/or producing novel antibodies targeting an emerging pathogen, preclinical, manufacturing, regulatory activities and clinical study start up activities to enable lead antibody selection through IND filing; followed by activities through clinical development in a Ph1a/NHV trial and, for the influenza program, a Phase 1b clinical study in adults for the treatment of uncomplicated influenza.

The scope of work will focus on a list of targets and include development of novel monoclonal antibodies for PEP, EP or REP. Influenza will be the top priority and first pathogen, while the remainder of the list and the priority of the other pathogens will be determined by the Oversight Committee and agreed by Regeneron and may include up to three BSL-4 pathogens.

The scope of work has been broken into a Base Period and five potential Option Periods for each targeted pathogen, with a Base Period covering influenza being established upon award of this Agreement:

- Base Period (CLIN1): Generation and isolation and characterization of lead mAbs and generation of (humanized) mouse model for PEP, EP and REP
- Option Period 1 (CLIN2): PMPD Ab Production and in-vivo testing of lead mAbs
- Option Period 2 (CLIN3): Toxicology
- Option Period 3 (CLIN4): IND Enabling Activities
- Option Period 4 (CLIN5): Clinical Study
- Option Period 5 (CLIN6): Additional Clinical Study

Option periods may overlap and will be triggered as described in the Go/No-Go Decision Gate Table.

The specific SOW items are based on current plans and are subject to modification under this Agreement as the development plan for each compound progresses and funding allocations are agreed upon between Regeneron and BARDA.

The SOW includes following activities: Generating, Validating, and/or Producing Novel Antibodies, Lead Selection, Nonclinical Development (Nonclinical Tox and PK Studies, Assay Development, Formulation Development), Drug Supply and Manufacturing, Consortium Management, Regulatory and Clinical Activities to enable initiation of a Ph1a Clinical Study in Normal Healthy Volunteers (NHV).

Antibodies and animal models developed by others (e.g. members of the Consortium) can be entered into any of the activities described in the SOW after agreement with BARDA. Depending on their properties, antibodies developed by members of the Consortium or antibodies developed by Regeneron prior to initiation of this SOW (e.g. influenza antibodies) will be entered into the workflow in the appropriate CLIN segment after data review and agreement between BARDA and Regeneron.

In addition, work streams can be focused on technology development activities (e.g. optimizing immunization, antibody selection, antibody function, antibody delivery, antibody production/expression etc.) as required by the envisioned antibody mechanism of action against a given pathogen.

Regeneron shall provide program management support throughout.

Regeneron is open to discussing use of its proprietary antibodies for USG-funded contracts on a case-by-case basis which we envision will be brought to the JOC on an as needed basis and if Regeneron, in its sole discretion, agrees to make such antibodies available, then the terms of any such transaction will subject to a mutually-agreed separate written agreement.

1. **Base (CLIN1): Generation and isolation and characterization of lead mAbs and generation of (humanized) mouse model for pre-emerging, emerging and reemerging pathogens (WBS 1.0)**

Activities in the base (CLIN1) period include; generation of immunization and screening reagents, immunization of VelocImmune® mice with appropriate target(s) of virus, development of screening assays, development of effector function assays, isolation of mAbs specific for the virus target and selection of the lead mAb(s). Activities are also included to support development of appropriate animal models to be utilized for in-vivo testing.

A lead selection meeting shall be conducted by the Joint Oversight Committee at the conclusion of preclinical lead selection for influenza, emerging, reemerging, or pre-emerging pathogens. Data will be reviewed during such Lead Selection Meeting of the Joint Oversight Committee to determine progression to Nonclinical Development. Regeneron and BARDA must agree upon any lead candidate(s) to be progressed to Nonclinical Development. Prior to initiation of Clinical activities, a lead selection meeting shall be conducted by the Joint Oversight Committee at the conclusion of lead selection for influenza, emerging, reemerging, or pre-emerging pathogens. Data will be reviewed during such Lead Selection Meeting of the Joint Oversight Committee to determine progression to Clinical Studies. Regeneron and BARDA must agree upon any lead candidate(s) to be progressed to Clinical Studies.

1.1.Program Management

Regeneron shall provide for the following: The overall management, integration and coordination of all Agreement activities in support of multiple candidates, including a management, legal, administrative, and technical infrastructure and staff to ensure the efficient planning, initiation, coordination, Consortium management, regulatory support, implementation, direction, and reporting of all Agreement activities.

1.1.1. Joint Oversight Committee

1.1.1.1. A Joint Oversight Committee (JOC) consisting of Regeneron and BARDA and a component of the Joint Oversight Committee, will meet quarterly at a minimum to mutually evaluate risks and progress of assets covered under this Agreement, endorse potential new assets and agree on modifications to the allocation of funding across activities covered under the Agreement. The JOC will also evaluate achievement of Portfolio Progress Milestones.

1.1.1.2. Regeneron may propose the replacement of molecules with backup molecules from its ongoing research programs. Such a proposal would require approval of the Joint Oversight Committee. With support from the JOC, Regeneron may also consider in-licensing candidates or adding consortium members to supplement the program's portfolio for influenza, emerging, reemerging, or pre-emerging pathogen medical countermeasures. Any proposal for Regeneron backup molecules or in-licensed candidates would take into account the probability of successful licensing of an in-licensed candidate and the outcome of development studies already performed under the program.

1.1.1.3. The Consortium shall perform activities in support of multiple candidates for influenza, emerging, reemerging, or pre-emerging pathogens, including, but

not limited to: contribution of technical expertise to plan, execute, and close out non-clinical studies; day-to-day oversight of subcontracted non-clinical activities; routine communication with BARDA and the Consortium regarding non-clinical activities; audits of any needed subcontractors; preparation of study reports; and preparation for as well as attendance at meetings concerning non-clinical results and plans. The Consortium shall perform activities including, but not limited to, in vitro and in vivo studies, resistance monitoring, and surveillance studies.

1.1.1.4. Project Review Meetings

1.1.1.5. At the discretion of the joint oversight committee Regeneron shall participate in teleconferences at least bi-weekly (every other week) or as otherwise agreed by the Parties, between the Consortium and BARDA to review technical progress. Teleconferences or additional face-to-face meetings shall be more frequent at the request of BARDA.

1.1.1.6. Regeneron and BARDA shall participate in kick-off and quarterly meetings to coordinate the performance of the Agreement. These meetings may include face-to-face meetings with BARDA/AMCG in Washington, D.C. and at work sites of the Consortium. Such meetings may include, but are not limited to, meeting of the Consortium to discuss study designs, site visits, technical, financial, regulatory and ethical aspects of the program.

1.1.1.7. On an annual or event driven basis, prior to the exercise of Agreement options, BARDA will invite Regeneron to give a presentation at an In Process Review Meeting attended by BARDA, AMCG, and select, invited interagency representatives and other interested parties, as needed.

1.1.1.8. Integrated Master Plan

1.1.1.9. Work Breakdown Structure (WBS): Regeneron shall utilize a WBS template agreed upon by BARDA for reporting on the agreement. Regeneron shall expand and delineate the Agreement Work Breakdown Structure (AWBS) to a level agreed upon by BARDA as part of their Integrated Master Plan for agreement reporting. The AWBS shall be discernible and consistent. BARDA may require Regeneron to furnish WBS data at the work package level or at a lower level if there is significant complexity and risk associated with the task.

1.1.1.10. Portfolio Performance Metrics: The Integrated Master Schedule outlines key milestones with "Go/No Go" decision criteria (entrance and exit criteria for each phase of the project).

2. Option 1 (CLIN2): PMPD Ab Production and in-vivo testing of lead mAbs

2.1. Activities in the Option 1 (CLIN2) period include utilizing the Speed-to-Clinic platform approach for production of material for preclinical toxicology studies for influenza,

emerging, reemerging, or pre-emerging pathogens and development of a tech transfer package, transfer process, including man-in-plant activities.

2.2. Activities in the Option 1 (CLIN2) period also include; performing in vivo efficacy studies to assess efficacy of candidate antibody in a suitable animal model of disease, including but not limited to therapeutic dose determination and modeling. Additionally, activities will include evaluation of individual monoclonal antibodies and cocktails of monoclonal antibodies in prophylactic and therapeutic models of respiratory virus infections in collaboration with Consortium Members.

3. Option 2 (CLIN3): Toxicology

Activities in the Option 2 (CLIN3) period include assay development activities to support nonclinical and clinical PK evaluation, GLP toxicology and tissue cross-reactivity (TCR) studies, and Nonclinical PK studies.

Regeneron shall perform activities in support of multiple candidates for influenza, emerging, reemerging, or pre-emerging pathogens, including, but not limited to: lead selection and optimization, technical expertise to plan, execute, and close out toxicology studies; day-to-day oversight of toxicology activities; routine communication with BARDA and the consortium members regarding toxicology activities; audits of any required subcontractors; preparation of study reports; and preparation for as well as attendance at toxicology-related meetings. These studies may be GLP and/or non-GLP studies that are required for the characterization of the non-clinical safety assessment of the antibody or ADC.

4. Option 3 (CLIN4): IND Enabling Activities

Activities in the Option 3 (CLIN4) period include clinical manufacturing, including all production, process and analytical activities required to establish Cell Banks, Drug Substance and Bulk Placebo manufacture, filling of Drug & Placebo Product, supply of clinical studies with Labeled Drug and Placebo Product, and execution of all related stability studies for Drug Substance and Drug Product.

Regulatory activities include preparing materials (meeting request, briefing document, meeting preparation) for the FDA and engaging the FDA in phase-appropriate planning.

Prepare documents and submit the IND with clinical trial protocol(s). IND amendments will be submitted as needed to support the clinical trial program.

5. Option 4 (CLIN5): Clinical Study

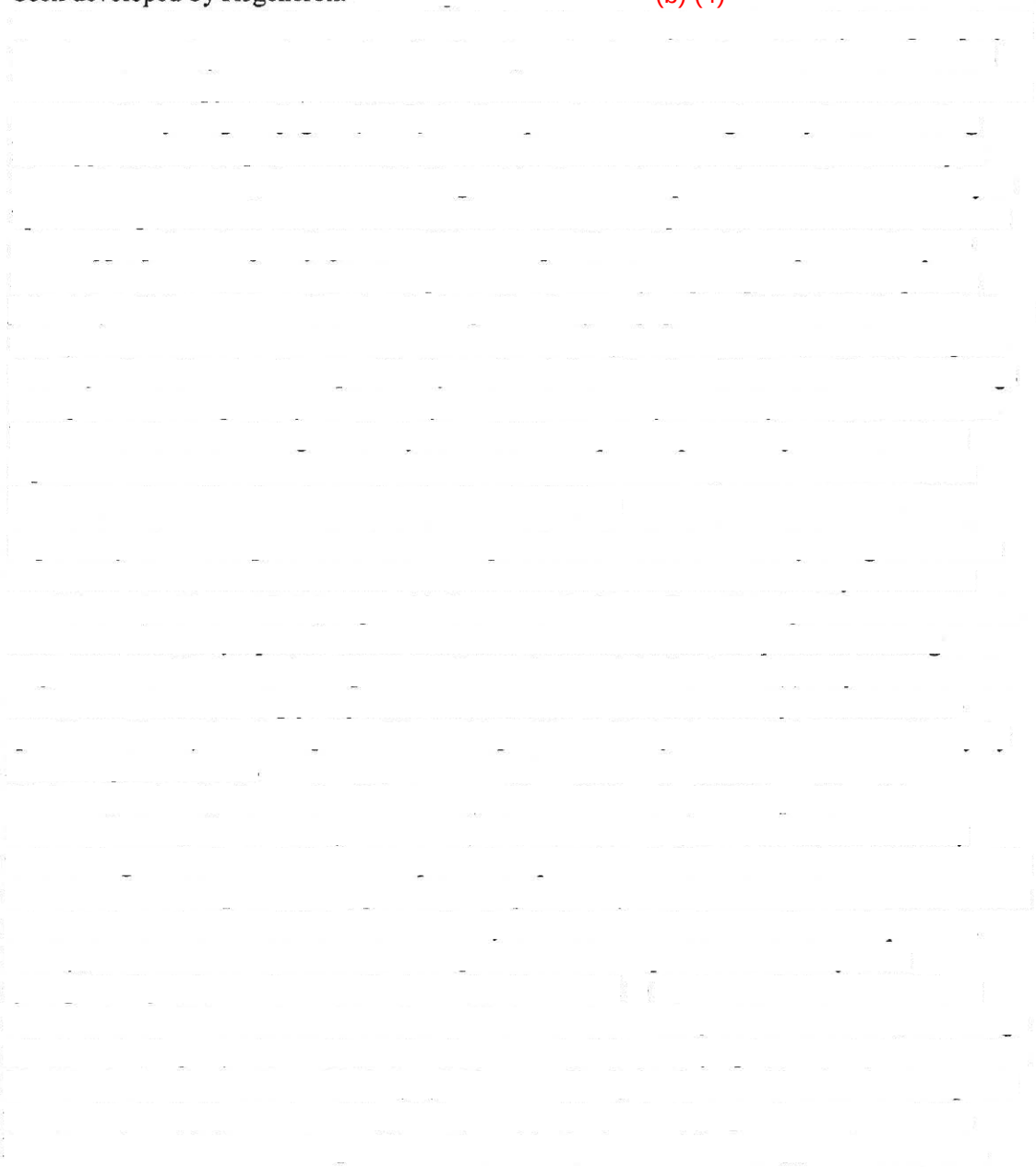
Activities in the Option 4 (CLIN5) period include performing Phase 1a clinical studies to provide safety information for product including dosage, pharmacokinetics, treatment duration, safety and tolerability as they relate to particular disease setting. Perform clinical sample analysis.

6. Option 5 (CLIN6): Additional Clinical Study

Activities in the Option 5 (CLIN6) period are intended for influenza only, and include performing Phase 1b clinical study for safety and tolerability of Influenza antibody or ADC in healthy adults with uncomplicated acute influenza infection

Preliminary plan for development of influenza therapeutics.

The objective of the influenza program is to select second-generation mAbs with superior properties to first-generation leads: antibodies recognizing group 1 influenza A virus hemagglutinin HA and antibodies recognizing group 2 influenza A virus HA that have already been developed by Regeneron. (b) (4)



Upon initiation of this SOW, current data generated with the Regeneron influenza antibodies will be reviewed by BARDA and Regeneron and selected lead molecules will be entered into the workflow in the appropriate CLIN.